REMARKS

Claims 1, 20, 22, 24, 26, 28, 31, 34, 37, 40, and 46 are pending in this application. Claims 22, 24, 26, 28, 31, 34, 37 and 40 have been withdrawn from consideration. Claims 1, 20 and 46 have been rejected. Claims 1, 20, 22, 24, 26, 28, 31, 34, 37, 40 and 46 have been canceled. Claims 51 and 52 have been added. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Election/Restriction Requirement Under 35 U.S.C. §121

The Examiner has indicated that Applicants arguments filed November 28, 2006 have been persuasive in so far as Groups I and VI are concerned. However, the restriction requirement placing the claims into Groups I-V has been deemed proper and made final. Claims 22, 24, 26, 28, 31, 34, 37 and 40 have been withdrawn from further consideration. Applicants respectfully disagree with the Examiner's reasoning for maintaining the restriction requirement for Groups 3, 4, and 5. However, in the interest of facilitating the prosecution of this application, Applicants have canceled claims 22, 24, 26, 28, 31, 34, 37 and 40 without prejudice, reserving the right to file continuing applications for the canceled subject matter.

II. Rejection of Claims Under 35 U.S.C. §112

Claims 1, 20 and 46 have been rejected under 35 U.S.C. 112, first paragraph, because it is suggested that the specification while being enabling for a method of inducing differentiation of an isolated human or rat marrow stromal cell into a pancreatic, insulin-producing cell, said method comprising contacting said

isolated marrow stromal cell with DMEM/20% FBS/1 mM beta-mercaptoethanol, and then cultured in DMEM/20% FBS/10 ng/ml bFGF, does not reasonably provide enablement for a method of inducing differentiation of an isolated MSC from any species of animal into other endodermal cells and other pancreatic cells that do not produce insulin. It is suggested that that the specification teaches differentiation of MSCs into pancreatic cells that secrete insulin, but the specification does not provide guidance for an artisan to arrive at the full breadth of any endodermal cell given that endodermal cells include any pancreatic cell, liver, lung or gut cell. It is further suggested that the breadth of the claims read on MSC obtained from any species of animal, but that art at the time of filing teaches that cells from different species of animal do not behave the same way. The Examiner cites Thomas et al. ((1999) *Endocrinology* 140:5036-5044) as teaching that in a rodent model of stromal cells, IGF-1 was effective in stimulating DNA synthesis with limited stimulation of type I collagen expression, whereas both IGF-1 and IGF-2 exerted proliferative effects, but inhibited collagen production in primary cultures of human marrow stromal cells. It is suggested that the teachings of Thomas et al. indicate that biological processes in cells are not predictably conserved between species of animals. The Examiner concludes, however, that the specification teaches that the steps used to arrive at pancreatic insulin-secreting cells can be practiced in rat and human cells, but the specification provides no guidance for practicing the method in other animals. Applicants respectfully disagree with this rejection.

At the outset, Applicants respectfully wish to point out that the Examiner's argument regarding enablement of any species of MSC

is not consistent. On the one hand, the Examiner has indicated that, based upon the teachings of Thomas et al., biological processes in cells are not predictably conserved between species such as rats and humans (the rodents referred to by Thomas et al. at the last line of column 1, page 5036, are rats as evidenced by the title of reference 21, "Effect of platelet-derived growth factor on DNA synthesis and gene expression in bone marrow stromal cells derived from adult and old rats"). On the other hand, the Examiner has acknowledged that the specification teaches that the steps used to arrive at pancreatic insulin-secreting cells can be practiced in rat and human cells. Therefore, Applicants have demonstrated that the two species of cells, which the Examiner cites as behaving differently, do in fact behave predictably in the instant method. Therefore, the rejection lacks any rationale for why the claims would not be enabled for MSC obtained from any species of animal.

Applicants also respectfully disagree with the Examiner's suggestion that the specification is not enabled for the full breadth of any endodermal cell. However, in the interest of facilitating the prosecution of this application, Applicants have canceled claims 1, 20, and 46 and present new claims 51 and 52 which read on the production of an insulin secreting pancreatic islet cell by contacting an MSC with an antioxidant and contacting the resulting endodermal/neuronal precursor cell with a growth factor. Support for this amendment is found throughout the specification and in particular at pages 21-23. In light of this amendment and accompanying remarks it is respectfully requested that this rejection be reconsidered and withdrawn.

III. Rejection of Claims Under 35 U.S.C. §102

Claims 1, 20, and 46 have been rejected under 35 U.S.C. 102(b) as being anticipated by Woodbury et al. ((2000) *J. Neurosci. Res.* 61:364-370). It is suggested that Woodbury et al. teach the induction of differentiation of rat and human bone marrow stromal cells (MSCs) by culturing the MSCs in the presence of DMEM/20% FBS/1 mM beta-mercaptoethanol. (BME) and then culturing the cells in DMEM/20% FBS/10 ng/mL bFGF (Woodbury et al., page 365, 1st column under "Neural Induction" and under "Quantitation of Neuronal Differentiation"). The Examiner acknowledges that Woodbury et al. teach that the MSCs differentiate into neuronal cells, however, because the two culturing steps taught by Woodbury et al. are the same steps used to arrive at the pancreatic cells of the present invention, Woodbury et al. inherently produced insulin-secreting pancreatic islet cells. Applicants respectfully traverse this rejection.

In accordance with the present invention, contact of a MSC with at least one antioxidant (*e.g.*, beta-mercaptoethanol, dimethylsulfoxide, butylated hydroxytoluene, butylated hydroxyanisole, ascorbic acid dimethylfumarate, or n-acetylcysteine; page 22, lines 9-12) results in differentiation of the MSC into a endodermal/neuronal precursor cell, wherein subsequent contact of the endodermal/neuronal precursor cell with a growth factor (*e.g.*, bFGF, insulin-like growth factor, epidermal growth factor or nicotinamide; see page 23, lines 20-23) results in the induction of an insulin secreting pancreatic islet cell. See pages 21-23. No such method is disclosed by Woodbury et al.

What Woodbury et al. do teach is several different methods for inducing neuronal differentiation. One method involves contacting

rat or human MSC with BME or alternatively DMSO/BHA. See the paragraph under the heading "Neuronal Induction" at column 1 of page 365. While this method provided differentiated neurons in excess of 50% (see the paragraph under the heading "Quantitation of Neuronal Differentiation" at column 2 of page 367), a second method was developed which involved the steps of 1) contacting rat MSCs with bFGF and 2) inducing neuronal differentiation with DMSO/BHA. See the paragraph under the heading "Quantitation of Neuronal Differentiation" at column 1 of page 365. By subjecting rat MSCs to the second method, the majority of the MSCs exhibited neuronal morphologies and stained positive for NSE (~78.2%) and NF-M (~79.2%) expression. See the paragraph under the heading "Quantitation of Neuronal Differentiation" at column 2 of page 367.

To anticipate a claim "every element of the claimed invention must be identically shown in a single reference." *In re Bond*, 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). Because Woodbury et al. do not teach or suggest the use of an antioxidant and a growth factor in the order claimed, this reference does not inherently teach the production of an insulin secreting pancreatic islet cell from an MSC. Accordingly, this reference cannot be held to anticipate the instant methods. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

IV. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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